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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/187,385	11/06/1998	SVETOMIR N. MARKOVIC	07039/119001	2986

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FISH & RICHARDSON P.C.
PO BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER

HOLLERAN, ANNE L

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 05/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/187,385	Applicant(s) MARKOVIC, SVETOMIR N.	
	Examiner Anne Holleran	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 February 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 30, 36 and 37 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 30 is/are allowed.
- 6) ☒ Claim(s) 36 and 37 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>10/18/2004</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The amendment filed February 3, 2005 is acknowledged. Claims 8, 12, 18, 21, 22, 26, 27, 31, 32, 35, 38 and 41-56 were canceled.

2. Claims 30, 36 and 37 are pending and examined on the merits.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections Withdrawn:

4. The rejection of claims 41-56 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the amendment canceling the claims.

5. The rejection of claims 26, 8, 12, and 22 under 35 U.S.C. 103(a) as being unpatentable over Edwards (Edwards, B.S. et al, J. Clin. Invest., 75: 1908-1913, 1985; cited in the IDS) in view of Hellstrand (U.S. Patent 6,063,373; issued May 16, 2000; effective filing date of Aug. 8, 1994) is withdrawn in view of the amendment canceling the claims.

6. The rejection of claims 26, and 21 under 35 U.S.C. 103(a) as being unpatentable over Edwards (Edwards, B.S. et al, J. Clin. Invest., 75: 1908-1913, 1985; cited in the IDS) in view of Hellstrand (U.S. Patent 6,063,373; issued May 16, 2000; effective filing date of Aug. 8, 1994)

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and further in view of Brittenden (Brittenden, J. et al, Cancer , 77: 1226-1243, 1996; of record) is withdrawn in view of the amendment canceling the claims.

7. The rejection of claims 27, 31, 32, 35, and 38 under 35 U.S.C. 103(a) as being unpatentable over Edwards (Edwards, B.S. et al, J. Clin. Invest., 75: 1908-1913, 1985; cited in the IDS) in view of Nichols (Nichols, P.H. et al. Clin. Exp. Immunol. 94: 4-10, 1993) is withdrawn in view of the amendment canceling the claims.

New Grounds of Rejection:

8. Claims 36 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kokoschka (Kokoschka, E.-M. et al., J. Invest. Dermatol. 95: 193S-197S, 1990) in view of Edwards (Edwards, B.S. et al, J. Clin. Invest., 75: 1908-1913, 1985; cited in the IDS).

Claim 36 is drawn to a method for stimulating the immune system of a human patient having a resectable malignant tumor comprising determining the natural killer lymphocyte cytotoxicity of said patient to provide a baseline natural killer lymphocyte cytotoxicity; administering an immunostimulatory dosage of an α -interferon composition to said patient, wherein said immunostimulatory dosage increases NK lymphocyte cytotoxicity at least about 75% above said baseline natural killer lymphocyte cytotoxicity; and surgically resecting said malignant tumor, wherein said malignant tumor is an early stage solid tumor. Claim 37 is drawn to a method for stimulating the immune system of a human patient having a resectable malignant tumor comprising determining the natural killer lymphocyte cytotoxicity of said patient to provide a baseline natural killer lymphocyte cytotoxicity; administering an immunostimulatory

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dosage of an α -interferon composition to said patient, wherein said immunostimulatory dosage increases NK lymphocyte cytotoxicity at least about 75% above said baseline natural killer lymphocyte cytotoxicity; and surgically resecting said malignant tumor, wherein said malignant tumor is melanoma.

Kokoschka teaches a method of treating stage I and stage II melanoma patients by surgical resection and then administration of recombinant interferon- α (rIFN- α) (see abstract). For entry into the study, patients had to be without evidence of residual disease at local and distant sites after surgery (page 194S, 1st col.). The specification defines early-stage solid tumor (page 8-9) as a solid tumor for which surgical resection results in a complete removal of detectable tumor tissue in a patient by current imaging techniques. Therefore, Kokoschka appears to teach surgery of early-stage tumors. Kokoschka teaches that patients with high-risk metastatic melanoma might benefit from long-term interferon- α therapy because interferon- α has immunodulatory effects such as the stimulation of natural killer cell cytotoxicity (see page 192S 1st-2nd col., bridging paragraph). Kokoschka fails to teach a method that includes the step of determining the natural killer lymphocyte cytotoxicity of a patient prior to the administration of interferon- α .

Edwards teaches a method for determining the optimal interferon- α dosage for the purpose of increasing NK lymphocyte cytotoxicity. Edwards finds that a peak NK cell activation, corresponding to a mean threefold increase above preinjection levels of NK cell activity results from injection of 3×10^6 U injected intramuscularly. Therefore, Edwards teaches a method of establishing a baseline NK lymphocyte cytotoxicity level and then injection of an immunostimulatory dosage of interferon- α increases NK lymphocyte cytotoxicity at least about

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75% above said baseline natural killer lymphocyte cytotoxicity. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the method of Edwards to determine the appropriate dosage of interferon- α for the treatment of cancer patients prior to surgery for the purpose of increasing the NK cell cytotoxicity in the method of Kokoschka. One would have been motivated to have combined the teachings of Edwards with Kokoschka because both teach that the usefulness of interferon- α in the treatment of cancer is the ability of interferon- α to increase NK cell activity and because both references appear to teach similar dose levels of interferon- α .

Conclusion

Claim 30 is allowed. Claims 36 and 37 are rejected.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (571) 272-0833. Examiner Holleran can normally be reached Monday through Friday, 9:00 am to 5:30 pm.

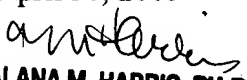
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 571-1600.

Anne L. Holleran

Patent Examiner

April 30, 2005


ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER